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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/762,550	02/09/2001	Akihiro Funakoshi	053466/0299	5276

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EXAMINER	
SPECTOR, LORRAINE	

ART UNIT	PAPER NUMBER
1647	8

DATE MAILED: 10/06/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/762,550	FUNAKOSHI ET AL.	
	Examiner	Art Unit	
	Lorraine Spector, Ph.D.	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Peri d f r Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disp sition of Claims

4)☒ Claim(s) 1-26 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-26 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5,6 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Part III: Detailed Office Action

Formal Matters:

References A3 and A6 on the information disclosure statement could not be considered; the former because there is insufficient identifying information on the PTO-1449 (No author, title or abstract number that would allow identification of which abstract applicants intended to cite), the latter because the document is in Japanese and no statement of relevance was provided.

Claim Interpretation:

Claims 1-11 are drawn to a "preventive or therapeutic agent for" pancreatitis, acute pancreatitis, or suppressing pancreatic edema. The intended use is given weight only to the extent that the art applied must be compatible with such intended use, and is not a use that must have been contemplated by the reference.

Objections and Rejections under 35 U.S.C. §112:

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 14-24 and 26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of treating pancreatitis or reducing pancreatic edema, does not reasonably provide enablement for preventing pancreatitis or total suppression of pancreatitis or pancreatic edema. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of

direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The nature of the invention is the use of anti-IL-6 modalities to suppress pancreatitis. The art (as cited below in the rejections over prior art) appreciates that IL-6 is an inflammatory cytokine that plays a role in the inflammation associated with acute pancreatitis as well as other manifestations of pancreatitis, such as breach of the blood-brain barrier. However, the art also teaches that there are multiple cytokines involved in acute pancreatitis and the inflammation that characterizes it. While the level of skill in the art is high, the person of ordinary skill in the art would not expect that suppression of the effects of a single cytokine would completely stop or prevent a condition that is due to the effects of multiple cytokines when, as in this case, the presence of IL-6 is not the initiating event (TNF is produced concomitantly, as are other inflammatory cytokines). The inventors have provided no guidance or working examples that would indicate otherwise. Accordingly, the invention is not enabled for prevention or total suppression of pancreatitis or the effects thereof.

Rejections Over Prior Art:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (f) he did not himself invent the subject matter sought to be patented.

Claims 1-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Kishimoto et al., EP 0 791 359 A1, cited by applicants.

Kishimoto et al. teach compositions for the prevention or remedy of diseases caused by IL-6, said compositions comprising antibodies against IL-6 receptors (IL-6R). Disclosed are monoclonal antibodies against both human and mouse IL-6R, recombinant antibodies, engineered antibodies, and humanized antibodies including humanized antibody PM-1, among others, see for example pages 2-3. The specifically claimed antibodies of claims 7 and 8 are disclosed; see page 4, page 5, and the claims. Kishimoto et al. are silent with respect to pancreatitis, acute pancreatitis and pancreatic edema. However, because the antibodies are disclosed for the use in treatment of IL-6 related conditions, the antibodies and compositions of Kishimoto et al. anticipate the claimed subject matter.

Claims 1-4 and 6-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Sato et al., Cancer Research 53(4):851-6, February 1993.

Sato et al. teach humanized antibody PM-1, which is an anti-human IL-6R antibody, and the use of such to inhibit IL-6 dependent tumor cell growth. Sato et al. are silent with respect to pancreatitis, acute pancreatitis and pancreatic edema. However, because the antibodies are disclosed for the use in treatment of IL-6 related conditions, the antibodies and compositions of Sato et al. anticipate the claimed subject matter.

Claims 1, 11-14, 24 and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Reed et al., Surgical Forum 48:179-180, 1997.

Reed et al. teach that administration of peptide YY (PYY) lowers early levels of circulating IL-6 in a model of necrotizing acute pancreatitis, and also reduces mortality in the model system. Accordingly, PYY is an IL-6 antagonist (as it lowered levels of IL-6). With respect to claims that specify suppression of pancreatic edema, such is inherent to the treatment of Reed et al.; if, as applicants allege, reduction of the effects of IL-6 has such effect, then such would have inherently occurred in the treatment of Reed et al.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness

rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 15-23 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reed et al., Surgical Forum 48:179-180, 1997, in view of Sato et al., Cancer Research 53(4):851-6, February 1993, and/or Kishimoto et al., EP 0 791 359 A1.

The teachings of all three references are discussed above. Reed et al. do not teach the use of anti-IL-6R antibodies for the suppression of IL-6 in necrotizing pancreatitis. However, in view of Reed's teaching that the suppression of such by PYY was beneficial in a necrotizing pancreatitis, it would have been obvious to the person of ordinary skill in the art at the time the invention was made to use the antibody compositions taught by Sato and /or Kishimoto et al. in the treatment of necrotizing pancreatitis. The person of ordinary skill in the art would have been motivated to do so by the teaching of Reed that reduction of IL-6 levels by PYY, and the teachings of the secondary references that the anti-IL-6R antibodies are useful for the treatment of conditions in which IL-6 is a factor. Accordingly, the invention, taken as a whole, is *prima facie* obvious over the cited art.

Claims 15- 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sato et al., Cancer Research 53(4):851-6, February 1993, and/or Kishimoto et al., EP 0 791 359 A1, either or both references in view of Gross et al., Hepato-Gastroenterol. 40:522-530, cited by applicants, and Farkas et al., Neuroscience Letters 242(3):147-150. 2/20/98.

The teachings of the primary references are discussed above. Both references teach the use of anti-IL-6R antibodies for the treatment of IL-6 related conditions. Neither reference teaches an association of IL-6 with acute pancreatitis.

Gross et al. teach that IL-6 concentrations are associated with acute pancreatitis; see page 525. Farkàs et al. teach that experimental acute pancreatitis results in increased blood-brain barrier permeability (title), and that such is associated with increased IL-6 levels (page 149, paragraph bridging columns). Accordingly, it would have been obvious to the person of ordinary skill in the art at the time the invention was made to use the compositions taught by Sato et al. or Kishimoto et al. to treat acute pancreatitis, in view of the teachings of Gross et al. and Farkas et al. The person of ordinary skill in the art would have expected success at doing so because the primary references teach the antibodies for the express purpose of inhibiting IL-6 associated responses. Accordingly, the invention, taken as a whole, is *prima facie* obvious over the cited art.

Advisory Information:

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Lorraine M. Spector, whose telephone number is (703) 308-1793. Dr. Spector can normally be reached Monday through Friday, 9:00 A.M. to 5:30 P.M.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Gary L. Kunz, at (703)308-4623.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist at telephone number (703) 308-0196.

Certain papers related to this application may be submitted to Group 1800 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Official papers filed by fax should be directed to (703) 872-9306 (before final rejection) or (703)872-9307 (after final). Faxed draft or informal communications with the examiner should be directed to (703) 746-5228.

Lorraine Spector

Lorraine Spector, Ph.D.
Primary Examiner

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9/25/03